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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,432	12/04/2003	Chichang Lee	CEN 5008 CIP	6872

27777 7590 02/16/2007

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/727,432	LEE ET AL	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) 15,16 and 18 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-14,17 and 19-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 6/17/2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants election with traverse of Group I. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Claims 1-21 are pending. Claims 15, 16 and 18, drawn to non-elected species are withdrawn from consideration at this time. Claims 1-14, 17 and 19-21 are examined on the merits.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 10/316,308, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The instant claim 1 encompasses the dependent claims 4 and 5. The '308 application does not describe the C504A cell line or cell lines "derived from" the Ag653 myeloma cell lines. Thus the '308 application fails to provide support for the instant scope of claim 1. Accordingly, claims 1-14, 17 and 19-21 will not be accorded priority to the earlier filing date consistent with that of the '308 application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite in the recitation of "phage displayed, transgenic mouse produced". It is unclear how the origin of the immunoglobulin or immunoglobulin fragment defines a functional or structural characteristic of the immunoglobulin or immunoglobulin fragment that can be differentiated for an immunoglobulin or immunoglobulin fragment not so produced.

Claim 9 is vague and indefinite in the recitation of "the immunoglobulin or fragment" which lacks specific antecedent basis in claim 6.

Claim 17 recites the "cell line obtained according to the method of claim 14". However, claim 14 is a method of producing a protein, not a method of obtaining a cell line. Thus it is unclear what claim 17 is intended to encompass.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 6-14, 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A)As drawn to a "derivative" of a myeloma cell.

Claims 1 and 6-13 and 19-21 are drawn to a clonal myeloma cell line capable of growing continuously ands at high density in a chemically defined medium, wherein said cell line remains viable after cyropreservation in the absence of serum. Claims 2 and 4are drawn to cell lines derived from the Sp2/0 myeloma cell line and the Ag653 cell line.. The claims encompass a genus of cell lines capable of growing to a high density in a chemically defined medium and

capable f remain viable after cytopreservation. However, the origin of the parent cell line does not serve to adequately describe the claimed derived cell lines, nor does Sp2/0 or Ag653 provide a nexus with the properties commensurate with a derivative of said cell lines because it is expected that the derived cell lines will have properties which differ from that of the parent cell line.. Derivation of cell lines relies on induced or spontaneous mutations or the accumulation of mutations. The art recognizes that mutations are random events and cannot be predicted. Thus the recitation of the name of a cell line and the origin of said cell line fails to provide an adequate description of the cell line because the cell line would be expected to have functional attributes which are not described or which differ from the parent Sp2/0 or Ag653 myeloma cell lines. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. One of skill in the art would reasonably conclude that applicant was not in possession of a genus of cell lines having the recited properties and derived from Sp2/0 cell or Ag653 cell beyond that of C463A cells and C540A cells.

(B) As drawn to immunoglobulins and fragments thereof which are "optimized, mutagenized, randomized, and recombined"

Claim 9 requires that the immunoglobulin or fragment produced from said cell be optimized, mutagenized, randomized and recombined. The disclosure of an immunoglobulin expressed from a C463A cell or a C504A cell does not adequately describe the genus of immunoglobulins or fragments thereof which are optimized, mutagenized, randomized or recombined because these procedure will produce an immunoglobulin which differs in structure from the immunoglobulin or fragment thereof which was expressed, and the result of optimized, mutagenized, randomized and recombined on any given protein structure cannot be predicted. Therefore there is no nexus between the structure of the expressed immunoglobulin and the structure of an optimized immunoglobulin. Further, there is no nexus between the structure or function of a mutagenized, randomized or recombined immunoglobulin and the parent immunoglobulin. Thus, the description of an expressed antibody does not adequately describe the claimed genus of antibodies.

Claims 3, 5 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of the C463A and C504A cell lines. It is not clear that a cell line possessing the identical properties of C463A and C504A are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Clark (Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man, 1993, pages 4-5) states

"The in vivo antibody response is heterogeneous and is made up of a large mixture of antibodies secreted from a polyclonal population of cells. In addition, because the differentiation of B cells involves the random rearrangements of gene segments and somatic mutation of these rearranged genes,....no two animals, even of an inbred strain will make an identical set of antibodies".

It is unclear that one of skill in the art could derive antibodies identical to those claimed. Undue experimentation would be required to generate and screen all of the possible antibody and hybridoma species to obtained the claimed antibodies without a publicly available source of the cell line or hybridomas which secreted the claimed antibodies. It is unclear that one of skill in the art could derive a cell line identical to that claimed. Undue experimentation without reasonable expectation of success would be required to screen all possible cell lines derived from Sp2/0 to obtain the C463A cell line and all possible cell lines derived from Ag653 because applicant has not described how said cell line was derived or the complete phenotype of the said cell lines. Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed cell line, a suitable deposit of C463Aand C504A for patent purposes, evidence of public availability of the claimed C463A cell line and C504A cell line or evidence of the reproducibility without undue experimentation of the claimed invention, is required.

If the cell lines are deposited under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposited cell lines have been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.
If the deposits are not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an

attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit. If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed. Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-3, 6, 7, 9 rejected under 35 U.S.C. 102(e) as being anticipated by Lee et al (WO 03/51720).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Lee et al disclose the C463A cell line, and the production of recombinant protein such as rTNV148B or infliximab or the production of other murine, chimeric , human, humanized, CDR grafted antibodies by introducing a exogenous nucleic acid into the C463A cell line by means of electroporation, lipofection, calcium phosphate precipitation, PEG precipitation, sonication, transfection, transduction, transformation or viral infection (page 2, lines 23-27, page 3, lines 8-33, page 32, lines 10-13 and page41, example 1). Lee et al disclose that the cC463A cell line continuously grew to high density in chemically defined medium (page 50, lines 7-16). Lee et al disclose the cell line wherein the immunoglobulin or fragment is selected from one or more of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2, sigA, IgD, IgE (page 3, lines 24-27). Lee et al disclose immunoglobulin fragments as F(ab')2, Fab', Fab,, Fc, Facb, pFc', Fd or Fv (page 3, lines 30-33). Lee et al disclose the production of recombinant protein at about 0.01 mg/L to about 10,000 mg/L or 0.1 pg/cell/day to about 100 ng/cell (page 5, line 32 to page 6, line 3).

Claims 1, 4, 6, 7, 12, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Pierard et al ('Secretion of Recombinant Hybrid Plasminogen Activators by Mouse myeloma', In: Advances in animal Cell Biology and Technology for Bioprocesses, Spier et al, Eds, 1989, pp. 475-480)

Pierard et al disclose a transformed AG653 cell growing to high density on serum-free medium, and the production of blood proteins such as u-PA and hybrid u-PA by transfection of the Ag653 cells with a plasmid encoding u-PA (page 475, lines 1-9 under the heading "Methodology and Results"). Pierard et al disclose the growth of the clones of each construction in serum free-medium (page 475, lines 23-25) and the production of the recombinant u-PA of up to 1.25 pg/cell/day (page 477, Table 3), which fulfills the specific limitations of the instant claims 12-14.. The reference does not specifically teach that the transformed Ag653 cells grown in serum free medium retain viability when cyropreserved in the absence of serum However, the claimed Ag653 serum-free adapted clones appears to be the same as the instant cell line derived from Ag653 in terms of growing to high density in chemically defined medium, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1, 2, 6, 7, 9, 10 and 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Newland et al (Biotechnology and Bioengineering, 1994, Vol. 43, pp. 434-438) as evidenced by the abstract of Shen et al (Animal Cell Technology, 1992, pp. 173-178).

Claim 1 is drawn to a myeloma cell line capable of growing continuously ands at high density in a chemically defined medium, wherein said cell line remains viable after cyropreservation in the absence of serum. Claim 2 embodies the cell line of claim 1 wherein said cell line is derived from the Sp2/0 myeloma cells. Claim 6 embodies the cell line of claim 1 wherein the genetic manipulation includes polyethylene glycol precipitation

Claim 7 embodies the cell line of claim 1, wherein the protein is selected from a group including immunoglobulins. Claim 9 embodies the cell line of claim 6 wherein the immunoglobulin is selected from a group including murine immunoglobulins. Claim 10 embodies the cell line of claim 7 wherein the immunoglobulin is selected from a group including an IgG1 antibody. Claims 12 and 13 require the production of the protein at about 0.01 mg/l to about 10,000 mg/L, and about 0.1 pg/cell/day to about 100 ng/cell/day.

Claim 14 is drawn to a method for producing atleast one protein from a cultured cell comprising culturing the cell line of claim 1 in a chemically defined medium, wherein the cells express on desired protein and isolating said desired protein from the chemically defined medium.

Newland et al disclose the Sp2/0-Ag14 derived hybridoma (SP01) (page 434, second column, line 1 under "Materials and Methods". Newland et al disclose the growth of the SP01 cells in chemically defined medium (Figure 1). Newland et al disclose the yield in monoclonal antibody production (Table I) that fulfill the specific embodiments of claims 12 and 13. The abstract of Shen et al discloses that the SP01 hybridoma produces an IgG1 antibody which is rodent, which fulfills the specific embodiments of claims 9 and 10. The reference does not specifically teach that the hybridoma cell retains viability when cyropreserved in the absence of serum However, the claimed hybridoma cells comprising the claimed antibody appears to be the same as the prior art antibody in terms of growing to high density in chemically defined medium, absent a showing of unobvious differences. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
2/5/2007